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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,650	11/09/2001	Hironori Tomi	44432.013600	6399

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EXAMINER
PATTEN, PATRICIA A

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/10/2002 5

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/031,650	Applicant(s) TOMI ET AL.	
	Examiner Patricia A Patten	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 15-30 is/are pending in the application.

4a) Of the above claim(s) 15,17,19-21 and 22-23 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 16,18,20,24,29 and 30 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 15, 17, 19, 23, 24, 27 and 28 drawn to a composition comprising *Withania sominifera* and a method for restoring compromised reproductive function with said composition.

Group II, claim(s) 16, 18, 20, 21, 22, 29 and 30 drawn to a composition comprising an extract of *Withania sominifera* and a method for restoring compromised reproductive function with said composition .

Group III, claim(s) 25 and 26, drawn to a method for preparing a composition comprising *Withania sominifera* Dunal extract.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I comprises the *Withania sominifera* whole plant, while Groups II and III constitute an extract of *Withania sominifera*. Because the definition of an extract is to 'separate' or 'pull out' some fraction of a plant, the claims lack the special technical feature regarding the other part(s) (fraction(s)) of the plant which was not 'extracted away' and thus the claims lack unity of invention.

During a telephone conversation with Eugene C. Rzucidlo on 8/15/02 a provisional election was made with traverse to prosecute the invention of Group II, claims 16, 18, 20, ~~21~~, 22, 29 and 30. Affirmation of this election must be made by applicant in replying to this Office action. Claims 15, 17, 19 and 23-28 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

PP 6/6/03

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Claims 16, 18, 20, 21, 22, 29 and 30 have been presented for examination on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 18, 20, 21, 29 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition/method comprising an ethanol or water extract of *Withania sominifera* for increasing sperm count, does not reasonably provide enablement for a composition/method comprising any extract of *W.sominifera* for restoring compromised reproductive function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective treatments for disease conditions are relatively rare, and may be

unbelievable in the absence of strong supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments.

In the instant case, Applicants have claimed a composition and method for 'restoring compromised reproductive function' comprising an extract of *Withania sominifera* Dunal. The following is an explanation of why 1) extracts of *Withania sominifera* Dunal are unpredictable and 2) why the claims are enabled for increasing sperm count, but not for restoring reproductive function.

The Instant specification has demonstrated that the ethanol extract from *Withania sominifera* Dunal is effective in increasing sperm count, however, has not clearly shown that said extract is effective in benefiting reproductive function. For example, Table 6 displays data which indicates that rats which were treated with *W.sominifera* after ethynylestradiol administration displayed an increased sperm count as compared to the group which only received the gum arabic control. However, there is *no substantial difference* in the motile sperm rate as indicated by the table, i.e., 55.9± 19.7 (gum arabic) and 57.1± 19.4 (*W.sominifera*).

Consequently, studies have been conducted in the art with regard to *W.sominifera* and reproductive function. For example, Garg et al. (1965) showed that feeding mice *W.sominifera* decreased litter size and even increased infertility rate in

male *and* female mice (Table 1, p.47). Thus, it can be concluded that the effectiveness of *W.sominifera* with regard to reproduction is questionable and unpredictable. There has been no nexus established between *W.sominifera*'s ability to increase sperm count and any benefits with regard to the etiology of reproduction in the prior art nor in the Instant specification. On the contrary, it appears that although *W.sominifera* may increase sperm count, the viability and reproductive nature of the sperm is highly questionable based upon data in the Instant specification as well as in Garg et al.

Further, it is deemed that the efficacy of different extracts of *W.sominifera* is unpredictable. Applicants have shown that ethanol extracts of *W.sominifera* are beneficial in increasing sperm count in rats, however, have not demonstrated wherein other extracts such as the pressed juice or an organic solvent extract would provide for similar effects (it is further known in the art that aqueous extracts of *W.sominifera* produce analogous effects, *infra*). It is well known in the herbal art that polarity of solvents plays a key role in determining the final product obtained by an extraction. However, because many phytochemicals remain undiscovered, the skilled artisan has to make his best educated guess as to what types of phytochemicals will be successfully extracted with a solvent of a particular polarity. Often times, unless the

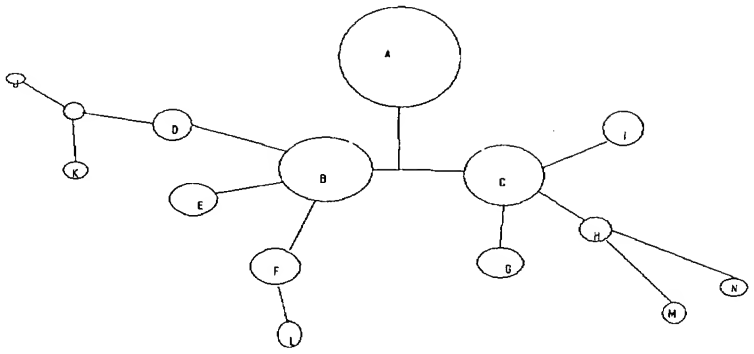
constituents in a particular plant extract have been well evaluated and documented in the literature, the skilled artisan must adhere to trial and error protocols in order to quantitatively determine phytochemical constituents present in samples obtained from respective extraction procedures. These procedures are common when, for example, a plant or part thereof has been documented in the literature as possessing some medicinal quality. The skilled artisan will carry out numerous tedious extraction protocols in attempting to isolate the particular ingredient(s) which has/have this medicinal quality. Typically, beginning with the first crude extraction, it is a guess as to weather or not the extract will possess the inherent medicinal quality. Take for example, the grape, *Vitis vinefera*. If this fruit was documented in the literature as having a particular medicinal qualities, the skilled artisan may feel the need to extract and isolate the medicinally beneficial ingredient(s)therefrom.

First, the skilled artisan would need to ascertain if the active ingredient(s) is/are found on the inside of the fruit; i.e., pulp or juice, or if alternatively, the active ingredient was found in the skin of the fruit. Thus, a first 'extract' may be obtained via pressing the fruit to obtain the juice and pulp of the fruit. The pulp and juice of the fruit would constitute a first product ('extract') with many various cell constituents. Of course, a determination would need to be made of if the extract, in this case, the pulp and the juice, actually possess the medicinal qualities as previously documented. If for example, the pulp and the juice of the grape did not prove to possess the documented

medicinal quality, the skilled artisan would then test the skin of the grape for said quality (commonly, prior to solvent extraction, homogenization of the solids occurs via blending or vortexing). If the skin of the grape actually possessed the documented quality, the skilled artisan may then attempt to purify the ingredient(s) further. Then, the skilled artisan will, by trial and error, attempt to perform step-wise extractions to isolate the active ingredient(s). If the first extraction attempt with a particular solvent fails, another solvent will be tried. Thus, beginning with the initial extraction, a first product is yielded which was extracted with the solvent, and a second product is yielded which remains because it did not possess a similar polarity to the solvent.

Each successive extraction yields different products due to the exclusion of ingredients based on the polarity of the solvents solvating constituents with similar polarities. Subsequently, *the properties of each respective product would need to be evaluated for efficacy.*

Above is an illustrative example of the many products which may be produced by different successive extraction protocols.



In this example, assume that A= the initial water extract from a homogenized sample of grape. The water extract from the grape is then subjected to a methanol/water extraction to form products B (soluble with methanol) and C (more soluble with water). Product C is then extracted in a separatory funnel with three organic solvents: chloroform, benzene and ethyl ether to form products G, H and I which solvate with the respective solvents based on the polarity of the inherent constituents. Product H, which we will assume is the product obtained in the benzene fraction, is extracted again in a separatory funnel with benzene and methanol to remove any residual methanol-soluble constituents. The additional circles represent extractions which may be done to obtain different products, using similar solvents as discussed previously, or entirely different solvents. Consequently, the properties of

each respective product would need to be evaluated for pharmacological efficacy. This representation is indicative of the vast array of distinct products which may be obtained due to the enormity of possible extraction permutations.

Additionally, according to the Stedman's dictionary 27th Ed, the term 'extract' means 'A concentrated preparation of a drug obtained by removing the active constituents of the drug with suitable solvents...'. Thus, purification of any of these products in the illustrative example to yield a specific phytochemical would constitute an 'extract' judging from the definition provided by Stedman's Medical Dictionary. Therefore, resveratrol, a phytochemical inherent in grapes, is deemed to be an 'extract' of grapes since it is obtained by the process outlined in Stedman's. Therefore, each respective phytochemical found within grapes constitutes an extract once it is 'extracted' away from the rest of the grape's constituents. Here, the unpredictability with regard to the term 'extract' in the claims has grown exponentially.

Each product obtained from an extraction is unpredictable in nature. Even the most skilled of artisans would need to quantify each product for constituents as well as medicinal efficacy. Unpredictability with regard to plant extracts has been well documented in the art. Revilla et al. for example (1998) showed that the slightest variations in polarity of solvent and reaction time upon grape extraction, provided respective products with unique characteristic properties (See Tables 1, 2, 4, 5, 6 and

7). In turn, each product would possess varying pharmacological properties based upon their respective phytochemical constituents.

Thus, to practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner to ascertain what other extracts besides aqueous and alcoholic extracts of *W.sominifera* would increase sperm count, as well as which, *if any* extract from *W.sominifera* would actually increase reproductive function. This inventive contribution would involve tedious trial and error protocols without the expectaction of success for the reasons set forth *supra*.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation

to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 16, 18, 20, 21, 29 and 30 are rejected under 35 U.S.C. 102(a) as being anticipated by Abdel-Magied et al. Claims 16, 18, 20, 21, 29 and 30 are drawn to a composition for restoring reproductive function comprising an extract of *W.sominifera*, and methods for restoring reproductive function with said extracts. However, in the instant case, the claims were examined on the merits for their enabled scope; specifically, a composition for increasing sperm count and a method for increasing sperm count with a *W.sominifera* extract.

Abdel-Magied et al. Taught that aqeuous extracts from *W.sominifera* increased sperm count (p.3, col,2 and Table 1, p. 4). The extract was administered as an aqeuous solution to the stomach via a feeding tube and was thus considered a 'food'.

Thus, the composition was well known. Even when the claim is considered on the merits with the broad scope of the intended use, the composition is anticipated: Applicant is asked to review In re Hack, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). "When the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated" (MPEP 2100 pp. 2113).

Claims 16, 18, 20 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Chavali et al. (US 5,683,698). The nature of claims 16, 18, 20 and 21 were discussed *supra*.

As previously discussed, *W.sominifera* extracts were known at the time the Instant invention was made. Chavali et al. (US 5,683,698) for example, described a proceedure for the aqueous extraction of *W.sominifera* roots to produce a pharmacutical composition which was then filled into gel capsules (col.4, lines 47-59). 'Gel capsules' would have been consumed, thus making them a type of 'food.'

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Rao et al. (1978). The nature of claim 16 was discussed *supra*.

Rao et al. (1978) for example, taught ether and ethanol extracts of *W.sominifera* (pp.236-237).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Patricia Patten, whose telephone number is (703)308-1189. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CHRISTOPHER R. TATE
PRIMARY EXAMINER